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MECHANISM OF THE CONDENSATION OF NITRO ALKANES WITH ALDEHYDES[1]

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Priebs (1) in 1884 condensed benzaldehyde with nitromethane but ten years elapsed before Louis Henry and his pupils (2) carried out extensive study of this reaction and showed that this aldol-type condensation could be extended to aliphatic aldehydes with facility, that dehydration of the nitro alcohol could be prevented, and also that more than one mole of aldehyde could react with suitable nitro alkanes. After the discovery of vapor-phase nitration (3) made all the nitro alkanes potentially available, Vanderbilt and Hass (4) improved and extended Henry's methods. Kamlet (5) devised a useful method of carrying out the reaction when he introduced the expedient of preparing the bisulfite addition product of the aldehyde (benzaldehyde) and the sodium salt of the nitro alkane and causing them to react, a method which has also been extended in this laboratory.

All the prior work was chiefly concerned with ascertaining the limits and usefulness of the reaction rather than with its mechanism. This work is concerned with ascertaining the mechanism of the condensation.

As is the case in the usual aldol condensation, the formation of a nitro alcohol requires the presence of a catalyst. The reaction involved is the addition of one of the hydrogens (in this case a hydrogen from the carbon atom holding the nitro group) to the carbonyl group of the aldehyde.

A salt of a primary nitro paraffin may react directly and rapidly with an aldehyde to yield the salt of a nitro alcohol.

$$RCHO + CH_2{=}NO_2Na \rightarrow RCHOHCH{=}NO_2Na$$

According to the resonance concept, the carbon atom of the carbonyl group bears a partial positive charge while the negative charge of the nitronic anion exists partially on the alpha carbon atom. These carbon atoms therefore attract each other, and the condensation consists essentially in their union.

If a salt of a secondary nitro paraffin is employed, the situation is somewhat different. The equilibrium

$$R'CHO + R_2C{=}NO_2Na \rightleftarrows R'CHONaCR_2NO_2$$

can not proceed very far to the right because the tertiary nitro group present in the nitro alcohol can no longer form a salt. The alcoholic hydroxyl group is a much feebler acid than a nitronic acid. As soon as a little alkalinity is built up

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the reaction must stop. In fact, Vanderbilt and Hass (4) showed that such a nitro alcohol can be split practically quantitatively by adding an equivalent of base.

According to this concept of the reaction, the function of the bisulfite in the Kamlet process is to prevent this accumulation of base and thus to allow the reaction to proceed virtually to completion. The formation of an addition compound between the bisulfite and aldehyde is entirely a secondary matter and of no essential importance to the reaction. Therefore, the addition of any other substance sufficiently acidic to neutralize the solution should also bring about the reaction. Strong mineral acids, however, are known to yield aldehydes and ketones when they react with salts of nitronic acids and for this reason their use did not appear advisable, but a weaker acid such as acetic or carbonic seemed suitable.

To test this hypothesis the condensations have been carried out with several different materials serving as acidifying agents.

EXPERIMENTAL

The nitro paraffins used in this study were obtained from Commercial Solvents Corporation and, with the exception of nitromethane which contained a trace of water, were practically pure as received but, nevertheless, all of them were redistilled through a packed column filled with glass helices. The aldehydes were of the best commercial grade and each was distilled immediately before using.

All the condensations were carried out in the same general manner. An aldehyde and a weak acid were added simultaneously to a solution containing the salt of a nitronic acid. Reaction took place rapidly, accompanied by a slight evolution of heat. The nitro alcohols obtained were light amber oils with a characteristic pleasing odor. They boiled over a narrow range and their constants agreed well with those more carefully determined previously in this laboratory.

Condensation of 2-nitrobutane and n-butyraldehyde using sodium bisulfite as the acidifying agent. 2-Nitrobutane (103 g., 1 mole) was gradually added in small portions to a hot, agitated solution of sodium hydroxide (41 g., 1.025 mole) in 300 ml. of water. The nitro alkane dissolved slowly and it was necessary to warm the mixture to maintain it at 60°. At the same time, *n*-butyraldehyde (72 g., 1 mole) was dissolved in a solution of sodium bisulfite (115 g., 1.10 mole) in 400 ml. of water. Then, with agitator and reflux condenser in position and the temperature of the sodium nitrobutane solution at 60°, the solution of bisulfite addition product was slowly added over a period of approximately two hours, maintaining a temperature of 60°.

The reaction mixture, from which some oil had already separated, was agitated vigorously overnight. The orange-colored oil layer was separated, the aqueous layer was extracted with two 100-ml. portions of ether, and the ether solution was combined with the oil layer. The combined ether solutions were washed with sodium bisulfite solution to remove aldehyde. Ether was removed by evaporation and the residue was distilled. 3-Methyl-3-nitro-4-heptanol, 17 g., b. 117–119°. at 10 mm., resulted. Yield of nitro alcohol, 27.8%. Yield of the same alcohol by the Vanderbilt-Hass method, 40.0%.

Condensation of 2-nitropropane with n-butyraldehyde using acetic acid as the acidifying agent. 2-Nitropropane (45 g., 0.5 mole) was gradually added to a well agitated solution of sodium hydroxide (20.5 g., 0.52 mole) in 80 ml. of water. The temperature was not allowed to exceed 50°. When formation of the salt was complete, a mixture of *n*-butyraldehyde (43.2 g., 0.6 mole) and glacial acetic acid (32 g., 0.53 mole) was added dropwise over a period of forty-five minutes with good agitation. The suspension was agitated and maintained at 50° for two hours after the material had all been added. The solution was

cooled and the product was separated as already described. Light yellow, oily 2-methyl-2-nitro-1-hexanol, 24 g., b. 103–106° at 8 mm., resulted. Yield of the nitro alcohol, 86.2%; conversion 46%. Yield by the Vanderbilt-Hass method, 65%.

Using similar conditions and the same molar proportions, the following reactions were carried out with results as indicated.

NITRO PARAFFIN	ALDEHYDE	CONVERSION %	YIELD %	YIELD, METHOD OF VANDERBILT-HASS %
1-Nitropropane	*n*-Butyraldehyde	63.8	88.4	96.5
2-Nitropropane	*n*-Butyraldehyde	46.0	86.2	65.0
2-Nitropropane	Isobutyraldehyde	14.2	30.4	11.0
2-Nitrobutane	Isobutyraldehyde	9.2	36.4	3.0

Condensation of 2-nitropropane and n-butyraldehyde using carbon dioxide as the acidifying agent. The amounts were the same as indicated in the preceding experiment except that no acetic acid was used. Instead, the agitated solution of the salt of the nitro paraffin was warmed to 45° and carbon dioxide was passed into it. After the carbon dioxide (generated from dry-ice) had been bubbling in about one minute, addition of aldehyde was begun. It was added dropwise over about twenty minutes. After carbon dioxide had been passed into the mixture for about three hours, reaction appeared to be complete and the mixture was allowed to stand for about eighteen hours. The product was mixed with 400 ml. of water and extracted with two 30-ml. portions of ether. This was processed as already described and collected over the same boiling range; 2-methyl-2-nitro-3-hexanol, 44.3 g., resulted; conversion, 55.0%.

Condensation of nitroethane and benzaldehyde using carbon dioxide as the acidifying agent. Nitroethane (82.5 g., 1.1 moles) was dissolved in a solution of sodium hydroxide (45 g., 1.12 moles) in 100 ml. of water. The solution was cooled to 65° and benzaldehyde (106 g., 1 mole) was added. The suspension was stirred with a powerful agitator until a fine emulsion existed; then carbon dioxide was passed in at a fairly rapid rate. The temperature was allowed to rise to 75° and was maintained at that level for two hours. The mass was allowed to stand twenty-four hours. Then the semi-solid contents of the flask were poured into water to dissolve the precipitated sodium bicarbonate.

The oil layer was separated, the aqueous layer was extracted with ether, and the extract was added to the oil layer. This was processed in the usual way. 2-Nitro-1-phenyl-1-propanol, 85 g., b. 120–126° at 2 mm., resulted. Conversion to nitro alcohol, 48%; yield, 91%.

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SUMMARY

It has been found that nitro alcohols may be produced rapidly and in good yields by adding an acidic substance such as glacial acetic acid, sodium bisulfate or carbon dioxide (as well as the sodium bisulfite previously reported by Kamlet) to an aqueous solution containing a salt of a nitronic acid and also an aldehyde.

A mechanism for the condensation is proposed which postulates union between the positive carbon atom of the carbonyl group and the negative alpha carbon

atom of the nitronic anion. According to this hypothesis, the function of the acid is, in the case of primary nitro paraffins, to liberate the nitro alcohol from its salt and in the case of secondary nitro paraffins to prevent the accumulation of base which reverses the addition.

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